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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/570,909

03/29/2006

Carsten Hopf

14129-00001-US

1220

23416 7590 01/09/2007  
CONNOLLY BOVE LODGE & HUTZ, LLP  
P O BOX 2207  
WILMINGTON, DE 19899

EXAMINER

HILL, KEVIN KAI

ART UNIT

PAPER NUMBER

1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/09/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

Application No.

10/570,909

Applicant(s)

HOPF, CARSTEN

Examiner

Kevin K. Hill, Ph.D.

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 7-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7-11 is/are rejected.
- 7) ☒ Claim(s) 7-11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date Dec. 4, 2006.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **Detailed Action**

1. Applicant's response to the Requirement for Restriction, filed on November 21, 2006 is acknowledged.

Applicant has elected the invention of Group I, claim(s) 7-11, drawn to a method for identifying a gamma secretase and/or a beta secretase modulator, and a method for preparing a pharmaceutical composition for the treatment of neurodegenerative diseases.

Within Group I, Applicant has elected the species "i", an agent that modulates a gamma secretase, as recited in Claims 7, 10 and 11.

2. Election of Applicant's species was made with traverse.

Applicant argues that a search of all the species poses no undue burden on the Examiner.

Applicants' arguments have been fully considered but are not found persuasive. MPEP §803 states that "If the search and examination of all the claims in an application can be made without serious burden, the examiner must examine them on the merits, even though they include claims to independent or distinct inventions."

In the instant case a serious burden exists since each limitation, directed to a modulator of gamma secretase, beta secretase or both secretases, requires a separate, divergent, and non co-extensive search and examination of the patent and non-patent literature. For instance, a search and consideration of the prior art as it relates to gamma secretase would not be adequate to uncover prior art related to beta secretase

Further, a search and examination of all the claims directed to the embodiments involves different considerations of novelty, obviousness, written description, and enablement for each claim. In view of these requirements, it is the Examiner's position that searching and examining all of the claims including limitations to gamma and beta secretases in the same application presents a serious burden on the Examiner for the reasons given above and in the previous Restriction Requirement.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 7-11 are under consideration.

***Priority***

4. This application is a 371 of PCT/EP04/09771, filed September 2, 2004. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Certified copies of the following foreign applications have been provided:

EPO 03019642.2, filed September 5, 2003,  
PCT/EP2003/013980, filed December 10, 2003,  
EPO 04001895.4, filed January 29, 2004,  
EPO 04001894.7, filed January 29, 2004,  
EPO 04007447.8, filed March 26, 2004,  
PCT/EP2004/004891, filed May 7, 2004,  
PCT/EP2004/004889, filed May 7, 2004, and  
EPO 04018874.0, filed August 9, 2004.

The Examiner was unable to find support for the instant invention, namely a method for identifying a gamma secretase modulator comprising *identifying a FADS2-interacting molecule* [emphasis added] in EPO 03019642.2, PCT/EP2003/013980, EPO 04001895.4, and EPO 040018904.7. A keyword search of the terms "FAD" and "FADS2" failed to identify specific contemplation of FADS2-interacting molecules in these applications.

Support was found in application EPO 04007447.8. Accordingly, the effective priority date of the instant application is granted as March 26, 2004.

If Applicant believes the earlier applications provide support for this disclosure, Applicant should point out such support by page and line number in the reply to this Action.

### ***Information Disclosure Statement***

Applicant has filed an Information Disclosure Statement on December 4, 2006, which has been considered. The signed and initialed PTO Form 1449 is mailed with this action.

### ***Claim Objections***

**5. Claims 7-11 are objected to because of the following informalities:**

These claims each identify FADS2 and APP as polypeptides that may be used in the claimed invention. However, the claims do not first identify the polypeptides by their complete names prior to using their acronyms. The abbreviation should be spelled out in the first appearance of the claims and should be followed by the abbreviation in parentheses, e.g. Epidermal Growth Factor (EGF). Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**6. Claims 7-11 are rejected under 35 U.S.C. 112, second paragraph**, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to the use of an enormous genus of FADS2-interacting molecules. The specification discloses that a FADS2-interacting molecule binds, at least temporarily, to FADS2 (pg 3, last ¶). The omitted steps are: demonstrating how an artisan will ascertain that the molecule is, in fact, interacting with FADS2.

Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. **Claims 7-11 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Winther et al (WO 01/70993 A2, September 27, 2001) and Fechteler et al (WO 01/49871 A2, July 12, 2001).

The claims are drawn to a method for identifying a gamma secretase modulator, comprising the steps of identifying a FADS2-interacting molecule, wherein the FADS2-interacting molecule binds to, and inhibits FADS2, and determining whether the FADS2-interacting molecule is capable of modulating gamma secretase, as measured by the ability of amyloid precursor protein (APP) to be cleaved.

Winther et al teach a method for identifying a compound that inhibits the activity of delta-6-desaturase (also known in the art as FADS2, see pg 4, line 1 of the instant specification) (pg 3, [0028]). Winther et al teach that host systems in which the method(s) may be performed include *in vivo* and *in vitro* systems (pgs 14-15, [0166-1076]). Winther et al contemplate that potential agonists include small molecules that bind to FADS2 polypeptides, and thereby extinguish its activity, by prevent binding to cellular binding molecules, e.g. regions of FADS2 which contact other proteins and/or localize the FADS2 within a cell, and regions which bind substrate, such that normal activity is prevented (pgs 17-18, [0201-0204]). Winther et al teach a composition for the treatment of a lipid metabolism disorder, comprising a compound identified by the inventive method and a pharmaceutically acceptable carrier (pg 3, [0031]), wherein

contemplated disorders include neurodegenerative diseases such as Alzheimer's disease and diabetic neuropathy (pg 4, [0037]).

Winther et al do not teach the method step of determining whether the FADS2-interacting molecule is capable of modulating gamma secretase activity, as recited in Claims 7 and 10. However, at the time of the invention, Fechteler et al taught methods of finding inhibitors of membrane-based proteases, in particular gamma secretase (pg 1, [0002]; pg 4, [0062]). The compounds identified by the inventive method(s) are contemplated to be useful for the treatment of neurodegenerative disorders, e.g. Alzheimer's disease, Parkinson's disease and Huntington's chorea (pg 4, [0065]). Fechteler et al taught that the activity of gamma-secretase may be measured by the ability of gamma-secretase to cleave a reporter protein that comprises a fragment of amyloid  $\beta$ , specifically the C99 fragment (pg 3, [0040-0044]), or endogenous A $\beta$  polypeptides (pg 8, [0113-0114], Example 8).

It would have been obvious to one of ordinary skill in the art to modify the method of Winther et al as taught by Fechteler et al with a reasonable chance of success because Fechteler et al teaches methods of assaying for APP cleavage. An artisan would be motivated to make such modifications because gamma secretase is a holoenzyme comprising Presenilin, Nicastrin and Pen2 subunits, each of which are associated with FADS2, and thus a FADS2-interacting molecule that interferes with FADS2 activity or binding to cellular proteins would likely affect the formation of the gamma-secretase holoenzyme, as measured by gamma-secretase activity taught by Fechteler et al.

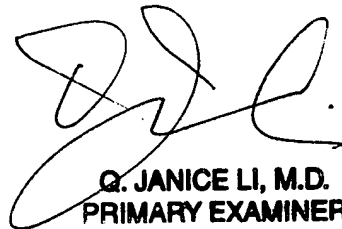

Thus, Claims 7-11 are *prima facie* obvious.

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



**Q. JANICE LI, M.D.**  
**PRIMARY EXAMINER**